

The Concentration of Serum Lipids and Protein Electrophoresis Fractions in Thyroid Disease Patients

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We analyzed and compared the concentration of total cholesterol (CHOL), high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol and triglyceride (TG) in serum and the serum protein electrophoresis fractions of thyroid disease patients. In comparison with the average of reference, our data showed that the average concentration of CHOL, LDL cholesterol and TG in hyperthyroidism patients were decreased significantly, but HDL cholesterol was increased significantly. In hypothyroidism patients, CHOL, HDL cholesterol, LDL cholesterol and TG were all increased significantly. In comparison of the concentration of lipids in each patient to reference range, 28.3% of hyperthyroidism patients showed abnormally low level of total cholesterol. In the patients with hypothyroidism, the percentage of patients showed abnormally high level of CHOL, HDL cholesterol, LDL cholesterol and TG were 37.7%, 10%, 68.8% and 49.1%, respectively. In our studies of serum protein electrophoresis, the average of α_2 -globulin and γ -globulin in hyperthyroidism patients were increased and β -globulin was decreased significantly. In hypothyroidism patients, the average of γ -globulin was increased and β -globulin was decreased significantly. In comparison of protein fractions of each patient to reference range, 38.3% and 50.0% of hyperthyroidism patients showed abnormally high levels of α_2 -globulin and γ -globulin, but 73.3% of patients showed abnormally low level of β -globulin. In hypothyroidism patients, 70.4% of patients were abnormally decreased in β -globulin and 63.9% of patients were abnormally increased in γ -globulin. These data suggest that the concentrations of CHOL, HDL cholesterol, LDL cholesterol and TG are not critical data for clinical interpretation of hyperthyroidism, but the levels of them are useful for interpretation of hypothyroidism patients. Our results of serum protein electrophoresis suggest that the concentration of serum protein electrophoresis fractions can be useful to understand the thyroid disease.

Key Words: Thyroid hormone, Cholesterol, Triglyceride, Protein electrophoresis

INTRODUCTION

The primary function of the thyroid is production of the hormones thyroxine (T₄), triiodothyronine (T₃), and calcitonin. These hormones regulate the rate of metabolism and affect the growth and rate of function of many other

systems in the body (Ekholm and Bjorkman, 1997; Oetting and Yen, 2007; Bianco et al., 2002). Thyroid disease occurs when the thyroid gland doesn't supply the proper amount of hormones needed by the body. If the thyroid is overactive, it releases too much thyroid hormone into the bloodstream, resulting in hyperthyroidism. An underactive thyroid produces too little thyroid hormone, resulting in hypothyroidism.

Hyperthyroidism causes the cells to speed up the metabolism activity, resulting in the body uses up energy more quickly than it should (Gharib et al., 2004; Surks and Hollowell, 2007; Fatourech, 2009). The amount of thyroid

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Table 1. Concentration of biochemicals in sera of patients (Mean \pm 2SD)

Biochemicals patients	Total cholesterol	HDL cholesterol	LDL cholesterol	Triglyceride
Reference	180.0 \pm 25.0	45.0 \pm 11.0	115.0 \pm 7.5	100.0 \pm 25.0
Hyperthyroidism	155.0 \pm 38.0	52.8 \pm 9.7	85.4 \pm 32.8	83.3 \pm 39.5
Hypothyroidism	242.4 \pm 44.0	58.0 \pm 13.3	150.0 \pm 37.8	172.9 \pm 43.8

hormones is controlled by the thyrotropin-releasing hormone (TRH) producing in hypothalamus and the thyroid-stimulating hormone (TSH) producing in pituitary (Sawin et al., 1985).

Hyperthyroidism and hypothyroidism are the most common problems of the thyroid gland. Measurement of the concentration of T3, T4, Free T4 (FT4) and TSH in the patient serum is the easiest and most reliable test for the diagnosis of thyroid function disease (Baskin et al., 2002). The normal ranges of T3, T4, FT4 and TSH are 0.8~2.2 μ g/L, 5~13 μ g/dL, 0.8~2.2 μ g/dL and 0.4~4.0 μ U/L, respectively (Hubner et al., 2002). Because of thyroid hormones regulate the metabolic activity of cells and organs, some previous studies were focused on the cardiac risk factors such as the concentration of cholesterol and triglyceride in serum and on the relation between liver function and thyroidism ((Kannel et al., 1964; Kannel et al., 1971; Key, 1975; Havel et al., 1980). These studies were designed to determine the effects of hyperthyroidism and hypothyroidism on the metabolism of lipids, glucose (Mary and Peter, 1981) and liver function (Fong et al., 1992), but did not study the effects of thyroidism on the concentration of serum protein electrophoresis fractions.

In this study, we compared the concentration of total cholesterol (CHOL), high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol and triglyceride (TG) in serum and serum protein electrophoresis fractions of thyroidism patients to understand the effect of thyroid hormone on the protein level in patient serum.

MATERIALS AND METHODS

Patients

A total of 121 patients aged 18 years and older with hyperthyroidism (n=60) or hypothyroidism (n=61). The

patients were selected from suspected thyroidism patients after analysis of T3, T4, FT4 and TSH. The group of hyperthyroidism patients were defined as ones showing higher levels of T3, T4, FT4 and lower level of TSH than those of people showing reference range. Also, the group of hypothyroidism patients were defined as ones showing lower levels of T3, T4, FT4 and higher level of TSH than those of reference range.

Serum Analysis

We analyzed the concentration of total protein (TP), CHOL, HDL cholesterol, LDL cholesterol and TG in serum of patient by Hitachi automatic clinical analyzer 7600 (Hitachi High-Technologies Co., Tokyo, Japan). Sera of patients were electrophoresized by using cellulose acetate membrane electrophoresis technique with Helena Laboratory electrophoresis system (Jeppsson *et al.*, 1979). Sera were loaded on the cellulose acetate membrane absorbed buffer. The membrane was run for 15 min. at 180 V and stained with Ponceau S. Fractions were analyzed with image analyzer (Vilber Lourmat, Cedex, France). The relative percent of the each protein fractions in serum was calculated and compared to reference range and each. All data were analyzed by SPSS software (Chicago, IL, USA).

RESULTS

A total of 121 patients suspected to be thyroidism were subjects of either hyperthyroidism (n=61) or hypothyroidism (n=60) in this study. We determined the concentration of CHOL, HDL cholesterol, LDL cholesterol and TG in sera of hyperthyroidism or hypothyroidism patients (Table 1), and compared the average concentration of each with the reference average (Fig. 1).

In comparison with the average of reference, the average

concentration of CHOL, LDL cholesterol and TG in sera of hyperthyroidism patients were significantly decreased by 14% ($P<0.01$), 26% ($P<0.01$) and 17% ($P<0.01$), respectively. But HDL cholesterol was increased by 17% ($P<0.01$). In hypothyroidism patients, the average concentration of CHOL, HDL cholesterol, LDL cholesterol and TG were increased 34% ($P<0.01$), 28% ($P<0.01$), 30% ($P<0.01$), and 72% ($P<0.01$), respectively.

The percentage of patients with hyperthyroidism or hypothyroidism showed abnormal levels of CHOL, HDL cholesterol, LDL cholesterol and TG were shown in Table 2. Among the patients with hyperthyroidism, 28.3% showed low level of total cholesterol. On the other hand, among the patients with hypothyroidism, the percentage of patients showing abnormally high level of CHOL, HDL cholesterol, LDL cholesterol and TG were 37.7%, 10%, 68.8%, and

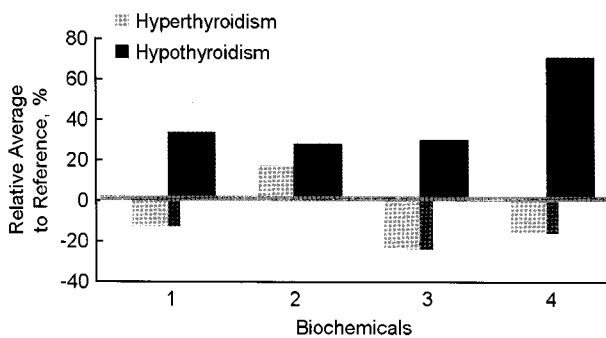


Fig. 1. The relative average concentration of total cholesterol (1), HDL cholesterol (2), LDL cholesterol (3) and triglyceride (4) in sera of hyperthyroidism and hypothyroidism patients to reference average.

Table 2. The patients (%) showed abnormal levels of biochemicals

Biochemicals Abnormal patients		Total cholesterol	HDL cholesterol	LDL cholesterol	Triglyceride
Hyperthyroidism	High	3.3	3.3	6.6	6.6
	Low	28.3	0	0	10
Hypothyroidism	High	37.7	10	68.8	49.1
	Low	0	0	0	3.2

Table 3. Concentration of total protein (g/dL) and protein electrophoresis fractions (%) in sera of patients (Mean \pm 2SD)

Biochemicals patients	Total protein	Albumin	α_1 -globulin	α_2 -globulin	β -globulin	γ -globulin
Reference	7.3 \pm 0.9	54.7 \pm 2.8	3.9 \pm 0.6	11.5 \pm 1.2	13.7 \pm 1.3	16.2 \pm 1.8
Hyperthyroidism	7.4 \pm 0.7	63.5 \pm 3.4	3.4 \pm 1.9	13.6 \pm 2.8	10.3 \pm 3.4	19.0 \pm 3.3
Hypothyroidism	8.2 \pm 0.7	54.8 \pm 7.4	3.1 \pm 2.2	10.7 \pm 2.7	10.9 \pm 4.0	20.3 \pm 5.4

49.1%, respectively.

The serum proteins of patients with thyroidism were also analyzed by using electrophoresis and the relative average concentrations of fractions to total protein (Table 3) were compared. When the averages of references were compared, the average of α_2 -globulin ($P<0.01$) and γ -globulin ($P<0.01$) in hyperthyroidism patients were increased, whereas β -globulin ($P<0.01$) was decreased significantly. On the other hand, the average of γ -globulin ($P<0.01$) was found to be increased, while β -globulin ($P<0.01$) was decreased significantly in hypothyroidism patients.

The percentage of patients with hyperthyroidism or hypothyroidism showing abnormal levels of albumin, α_1 -globulin, α_2 -globulin, β -globulin, and γ -globulin are shown in the Fig. 2 and Fig 3. In the hyperthyroidism patients, the patients showing abnormally high level of α_2 -globulin and γ -globulin were 38.3% and 50.0% respectively. In addition, 33% of patients and 73.3% of patients showed abnormally low level of the α_1 -globulin and β -globulin, respectively. On the other hand, the patients with hypothyroidism showing high level of albumin and γ -globulin were 21.3% and 63.9%. The hypothyroidism patients showing low level of albumin, α_1 -globulin, α_2 -globulin and β -globulin were 26.2%, 50.8%, 29.5% and 70.4%, respectively.

DISCUSSION

It was suggested that abnormal levels of thyroid stimulating hormone may represent a novel cardiac risk

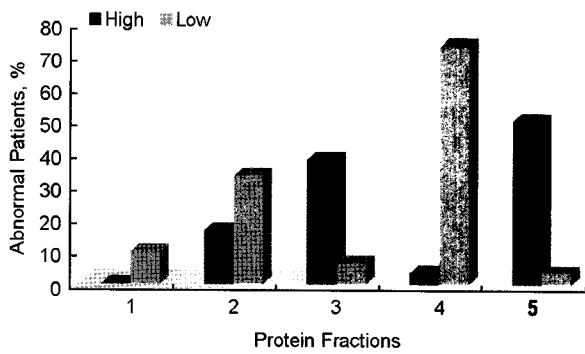


Fig. 2. The rate of patients showed abnormal level of albumin (1), α_1 -globulin (2), α_2 -globulin (3), β -globulin (4) and γ -globulin (5) fractions in sera of hyperthyroidism patients. The fractions were fractionated with cellulose membrane by electrophoresis method.

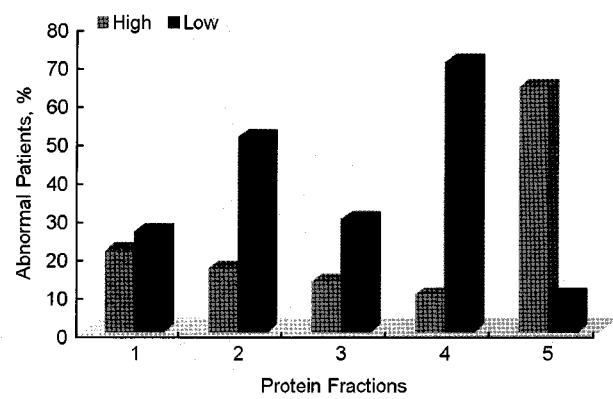


Fig. 3. The rate of patients showed abnormal level of albumin (1), α_1 -globulin (2), α_2 -globulin (3), β -globulin (4) and γ -globulin (5) fractions in sera of hypothyroidism patients. The fractions were fractionated with cellulose membrane by electrophoresis method.

factor in previous studies (Hak et al., 2000; Kvetny et al., 2004). Thyroid hormone excess and deficiency are common, as well as readily diagnosed and treated. Even mildly altered thyroid status affects serum cholesterol levels, risk of coronary artery disease, and cardiovascular mortality (Danese et al., 2000; Cappola et al., 2003). Previous studies have suggested that excess of thyroid hormones affects hypermetabolism, elevation of blood glycerol and ketone bodies due to increased lipolysis and ketogenesis (Harlan et al., 1963; Tibbling, 1969).

Our data showed that CHOL, LDL cholesterol and TG were decreased significantly except HDL cholesterol in hyperthyroidism patients. On the other hand, CHOL, HDL cholesterol, LDL cholesterol and TG in hypothyroidism patients were all increased significantly. These data are similar to previous reports which demonstrated the concentration of thyroid hormone in thyroidism patients affected the levels of CHOL, LDL cholesterol and TG (Kannel et al., 1971; Kvetny et al., 2004). However, previous studies did not demonstrate the HDL cholesterol. HDL cholesterol increase significantly in both hyperthyroidism and hypothyroidism patients. The level of HDL cholesterol in thyroidism patients does not seem to be correlated with thyroid hormone.

In comparison of protein fractions of each patient to reference range, A few patients of hyperthyroidism showed abnormal decrease except total cholesterol (28.3% of patients were decreased), but 37.7% (total cholesterol), 68.8% (LDL cholesterol) and 49.1% (TG) were shown

abnormal increase in hypothyroidism patients. These data suggest that the concentrations of CHOL, HDL cholesterol, LDL cholesterol and TG are not critical data for clinical interpretation of hyperthyroidism, but the levels of CHOL, LDL cholesterol and TG in hypothyroidism are useful for interpretation of thyroidism.

Electrophoresis of serum proteins is a commonly used clinical test. The patterns of fraction illustrate important pathological conditions. Previous investigators reported that decrease of albumin, increase of β -globulin and γ -globulin were shown in patients with liver disease and that decrease of albumin, increase of α_2 -globulin and γ -globulin were shown in patients with nephrotic syndrome (Jeppsson et al., 1979; Lewandrowski, 2002; Burtis et al., 2006). In our study, the concentration of protein fractions showed significant differences. The level of α_2 -globulin was increased significantly only in hyperthyroidism patients, whereas the levels of β -globulin and γ -globulin increased significantly in both hyperthyroidism patients and hypothyroidism patients. Previous studies have reported a higher prevalence of goiter and/or thyroid hormone abnormalities in persons with end-stage renal disease (Lim, 2001; Zoccali et al., 2005). Recently, there is a notice of the prevalence of subclinical and clinical primary hypothyroidism increased with progressively lower levels of kidney function in a nationally representative cohort of U.S. adults (Lo et al., 2005). Our data are not identical with the reports of previous studies. But in our study, comparison of protein fractions

of each patient to reference range showed that 38.3% (α_2 -globulin) and 50% (γ -globulin) of hyperthyroidism patients were abnormally increased and 73.3% of patients were abnormally decreased. In hypothyroidism patients, 70.4% of patients were abnormally decreased in β -globulin and 63.9% of patients were abnormally increased in γ -globulin. These data suggest that there is a significantly positive correlation between concentration of thyroid hormone and production of proteins affected by liver and kidney function.

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